OTGM 3 Outline

Ch 159A – Pain assessment and management in cognitively intact and impaired patients

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Ch 159A-01: Definition, epidemiology, aetiology and consequences of pain

The commonly used International Association for the Study of Pain (IASP) definition states that "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Bonica 1979). There are two main types of chronic pain, firstly nociceptive pain which results from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors. Those nociceptors can be located in somatic (e.g. skin, musculoskeletal tissues) or visceral tissues, causing somatic or visceral pain and secondly pain caused by a lesion or disease of the somatosensory nervous system which is called neuropathic pain. In the literature up to 40% of patients with cancer suffer with pain during the last three days of their life. Even in those without life-threatening illnesses like metastatic cancer, chronic pain affects 25%- 76% of home dwelling people over 65 years, and up to 93% of older people in nursing homes (American Geriatrics Society Panel 2009; British Geriatrics Society 2013). Epidemiological studies show that the most common causes are joint pain (knees in particular) and low back pain due to osteoarthritis, pain from previous fractures and, peripheral neuropathies (British Geriatrics Society 2013; Gibson and Lussier 2012).

Pain is often under recognised in the older population. This can be due to multiple chronic diseases whose symptoms mimic the pain. Moreover older people may be reluctant to consult due to the prevailing idea that pain is inevitably associated with ageing, are they may also fear of invasive tests and treatments (Davis and Srivastava 2003).

In older people with impaired cognition, the recognition of pain may be altered as well as the ability to communicate pain, resulting in a higher incidence of unrecognized and undertreated

pain. However, persistent pain has a significant impact on the quality of life of older people. It leads to decreased social activity and an increase in sleep disorders, under-nutrition, risk of falling, depression, anxiety, delirium and cognitive decline (Davis and Srivastava 2003; British Geriatrics Society 2013). It also increases costs and utilisation of healthcare (American Geriatrics Society Panel, 2009). Therefore adequate assessment and management of pain are necessary especially in the older population (see chapter 059-03).

Ch 159A-02: Neurophysiology and perception of pain

Ageing is associated with widespread changes in the cellular and neurochemical substrates of the nociceptive system. These include a decrease in density of unmyelinated and myelinated fibres; reduction in substance P, calcitonin gene-related peptide (CGRP) and somatostatin; serotonergic and noradrenergic neurons in the dorsal horn; and neuronal death and neurofibrillary abnormalities in the central nervous system.

The reduced efficacy of the endogenous analgesic systems together with the decline in afferent transmission pathways results in little or no change in acute pain perception. However, with an intense level of stimulation, any deficit in endogenous analgesia will become critical, thereby making it more difficult for older people to cope with severe or persistent pain conditions. Moreover, older patients demonstrate a much longer period of secondary hyperalgesia despite comparable levels of pain stimuli (Gibson and Farell 2004). This raises the possibility that older people may experience unnecessary persistence of painful symptoms associated with a prolonged resolution of sensitisation. Thus, previous ideas that older people are marginally insensitive to pain are no longer sustainable. Under circumstances where pain is caused by an intense stimuli or likely to persist, older people are especially vulnerable to the negative impacts of pain. Early and adequate treatment of acute pain should therefore be considered.

An interesting group of older people are those with cognitive impairment and/or dementia. Studies have shown that pain threshold of patients with Alzheimer's disease did not differ, whereas pain tolerance was significantly increased (Benedetti *et al.* 1999; Benedetti *et al.* 2004; Scherder *et al.* 2005). Also autonomic responses to pain, such as increases in heart rate, blood pressure, respiratory rate and sweating, seems to be altered in patients with chronic pain and also in those with Alzheimer's disease. Rainero and co-workers (2000) and later Benedetti et al. (2004) showed a negative correlation between heart rate responses and degree of cognitive impairment, in the presence of normal tactile and pain threshold. This finding indicates an altered autonomic response and is not the result of a decline in pain sensitivity. (Scherder 2013) Measurement of pain-related somato-sensory evoked potentials in patients with severe dementia showed that the processing of pain that involves areas of the medial pain system was impaired, although the pain stimulus itself was perceived adequately (lateral pain system) (Scherder 2013). Consequently, people with Alzheimer's disease may have difficulty understanding the meaning of the sensation and placing it in context. The prefrontal cortex has a role in the suppression of pain and therefore lesions of this part of the brain in dementia, may cause not only cause agitation/aggression but can also contribute to an increase in pain experience. This suggests another mechanism of how behavioural disturbances can be linked to pain. Moreover evidence for a causal relationship emerges from studies administering pain medication to patients with behavioural disturbances resulting in a decrease in aggressive behaviour (Husebo *et al*. 2014).

Ch 159A-03 Assessment of Pain and Discomfort

Assessing pain in older people

Comprehensive and detailed pain assessment is the cornerstone of managing pain in older people. This can be challenging in busy clinical environments where older people are further disadvantaged by complex chronic multi-morbidity visual, hearing and cognitive impairment.

Pain is a subjective and individual phenomenon and absolute quantification is impossible. The experience of pain and how it is reported by older people is also influenced by a complex range of social and psychological factors. For example, stoicism has been reported as an important influence in the under-reporting of pain in older people, it may affect pain reporting, and mediate the chronic pain experience in general (British Geriatrics Society 2013).

Clinical assessment

The principles of pain assessment in older people are the same as those underpinning any good quality clinical interaction. Better quality information on pain is gained by using "open" rather than "closed" questions, with minimal interruptions by the health professional (Royal College of Physicians 2007). Assessment should always begin with direct enquiry about whether pain is present and it is important to use alternative words and phrases for pain , for example "are you in pain?", "does it hurt?", "is it sore?", "do you have an ache?". The American Geriatric Society's 2002 Pain Guidelines give a useful summary of important clinical questions that should be used when assessing pain (AGS Panel on Persistent Pain 2002).

Observation, even in people who are able to describe their pain is key, are there signs of limitation of movement or function, how does the person, move or take their seat? This is especially important in older people who have difficulties with cognition or communication.

Questions about pain should include three key dimensions (Royal College of Physicians 2007):

1. The sensory dimension
    - *intensity*, using a standardised pain assessment scale (see below)
    - *character* or nature of the pain (e.g. sharp, dull, burning etc.)
    - *location* and radiation of the pain (by patients pointing to the pain on themselves or by using a pain map)

2. The affective dimension in terms of the person's emotional response to pain and how they perceive this, for example fear, anxiety or depression
3. The impact, to describe any disabling effects of pain on the person's function and activities of daily living and their ability to participate in work, social activities and relationships.

Standardised scales can be very helpful if presented in a clear and accessible format. There should then be a detailed physical examination to identify any treatable causes. However, it is important to be aware that pain can exist even when physical examination is normal.

Rating scales

Rating scales can be useful to help indicate the intensity of pain in older people (Chibnall and Tait 2001). Examples of these include the VRS section of the McGill questionnaire (Melzack 1987) and the NRS (van Dijk *et al.* 2012) which comprises a line marked with numbers 0–10 at equal intervals, where 0 is no pain and 10 is worst pain imaginable. Some people with mild or moderate cognitive impairment can also use verbal or numerical rating scales, particularly if they are given assistance (Pautex *et al.* 2005). These scales are valid and reliable in older people (Chibnall and Tait 2001, Herr *et al*. 2004). The use of visual scales can be optimised by using large lettering and ensuring that lighting is good. Once a scale is found which suits the person's abilities the same scale should be used for subsequent assessments to assess the response to interventions (Royal College of Physicians 2007).

Assessing pain in people with communication difficulties

The 'gold standard' for pain assessment is self-report. However this can be challenging for older people with cognitive impairment secondary to dementia and also those with strokes, Parkinson's disease or limited abilities with verbal communication. Cultural and language factors may also impair communication.

The general principles of pain assessment, as described above, apply but it is also vital to seek collateral history from a relative or caregiver. Detailed review of the medical and nursing notes may also reveal potential sources of pain. A multidisciplinary approach involving the assistance of speech and language therapist or psychologist can be very helpful. However, despite widely held beliefs to the contrary, many patients with moderate to severe dementia can report pain reliably (Zwakhalen *et al*. 2006). In those with communication difficulties it may be necessary to use direct observation or validated observational pain scales. Pain tools developed for this population include a range of items, many of which cover the AGS Guidelines (2002) which include a comprehensive range of potential indicators; facial expression, verbalization and vocalizations, body movements, changes in interpersonal interactions, changes in activity patterns or routines and mental status changes (AGS Panel on Persistent Pain 2002). They recognize the various ways in which pain or discomfort are being expressed and are based on the hypothesis that pain often manifests as behavioral change such as agitation, distress, social withdrawal, depression, or resistive behavior (Scherder *et al*. 2009).

The American Geriatrics Society (AGS) Panel on Persistent Pain in Older Persons (2002) recommends that a range of behavioural indicators should be considered in older adults with cognitive impairment. No observational pain tool is perfect and all have advantages and disadvantages but most items from most of these domains (table 1). Observational instruments with consistently positive assessments in reviews include the Abbey Pain Scale (Abbey), the DOLOPLUS2, the Pain Assessment in Advanced Dementia (PAINAD),and the Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC) (Hadjistavropoulos *et al*. Lancet neurology 2014).

Table 1. American Geriatric Society behavioural indicators of pain

	Domain	Example Behaviour
1	Facial expressions	frowning, rapid blinking
2	Verbalizations and vocalizations	moaning, grunting

3	Body movements	protecting sore areas, pacing
4	Changes in interpersonal interactions	disruptive behaviour, withdrawal
5	Changes in activity patterns or routines	changes in sleep or appetite
6	Mental status changes	increased confusion, crying

Ch 159A-04 Treatment of pain

There are only few randomized controlled trials available on the treatment of pain in a geriatric patient population. For this we will synthesize evidence and expert based guidelines from geriatric national organisations (American Geriatrics Society Panel 2009; British Geriatrics Society 2013).

Management of pain starts with an optimal assessment and detailed evaluation of pain as described previously. After assessment we consider following steps: non-pharmacological management, topical preparations, local (minimal) invasive treatment followed by systematic analgesics (Guay *et al*. 2002).

Non-pharmacological management

Non-pharmacological treatment includes education in self-management techniques for both the patient and his caregiver. Other non-pharmacological options are broadly discussed in the guideline of the British Geriatrics Society (2013). In summary, they suggest considering ways of increasing activity using exercise adapted to the preferences of the patient or the use of assisted devices such as walking aids, which may reduce pain intensity. There is limited to weak evidence that mindfulness, meditation, biofeedback training and relaxation can be useful in an older population. For the use of complementary therapies such as TENS, acupuncture, massage, aroma-therapy, and reflexology, there is also only limited evidence of effectiveness available (British Geriatrics Society 2013).

Topical preparations

Topical preparations are the second step available for the treatment for chronic pain in the older population. There is some evidence that short term treatment local NSAID therapy can be

helpful especially when pain is localized (Massey *et al.* 2010). There is less evidence available for the use of local lidocaine patches, although NICE guidelines recommend their use for localized treatment of neuropathic pain when older people are unable to take oral medication (British Geriatrics Society 2013).

Minimally invasive local therapy is recommended to manage pain even in palliative medicine. There may some benefit for epidural steroid injections for spinal stenosis in older patients, but there is no strong evidence for its use in radicular pain syndromes. There is weak evidence for the use of sympathectomy in neuropathic pain in older persons. For osteoarthritis of the knee in patients intolerant to systemic therapy, intra-articular (IA) corticosteroid injections could be considered. For patients with post herpetic neuralgia nerve block and botulinum toxin in patients may be effective.

Systemic analgesic treatment

Safe and efficient pharmacological treatment of pain in older people is a real challenge. Normal ageing causes well-characterised changes in the pharmacokinetics and pharmacodynamics of analgesic drugs. Due to the increased likelihood of polypharmacy together with a decrease in body water and lower concentration of plasma protein, the risk of drug interactions and iatrogenic effects is increased. Moreover a decrease in glomerular filtration rate leads to a decreased excretion of drugs their metabolites. This results in higher plasma concentrations of most drugs and higher toxicity. On the other hand, free fatty mass increases 15 to 20% causing lipid soluble drugs (fentanyl, diazepam) to have a higher distribution volume, needing more time to achieve a stable plasma concentration and more time to be eliminated. Receptor-level responses (pharmacodynamics) can also change with ageing. A higher sensitivity is seen at the μ, δ and κ -receptor, inducing an increased response to opioids.

To diminish the risk of adverse events in treating older people some general recommendations have been made by national geriatrics societies in the United Kingdom and the USA (British Geriatrics Society 2013; American Geriatrics Society 2009).

- Start low with one drug in a time and titrate the dose slowly to achieve response
- Use the least invasive route of administration (oral route is preferred if possible)
- Combination therapy using complementary drugs may have synergistic effects, be more effective at lower doses, thus reducing the risk of side effects
- In older patients with moderate to severe pain, give analgesics regularly, avoiding the use of PRN only
- Consider individualized therapy, taking into account comorbidity and other medication when choosing analgesia to minimise drug-drug interactions
- Medication should be initiated following the three steps of the WHO pain relief ladder (http://www.who.int/cancer/palliative/painladder/en/)

Additional recent papers give a comprehensive review concerning dose and adverse side effects for different available analgesics (Tracy and Morrison 2013; Atkinson *et al.* 2013).

Paracetamol/Acetaminophen : although there is little trial evidence in the older population, paracetamol/acetaminophen is recommended by most of the guidelines as an effective and safe analgesic for musculoskeletal pain and osteoarthritis. However, recent studies report a higher incidence of liver failure in low weight malnourished older people. So maximum tolerated dose should be reduced (lower than 4g/d) by people over the age of 65.

Non-steroidal anti-inflammatory drugs (NSAIDs): Although there is no direct evidence for the efficacy of NSAIDs in older people, evidence from younger populations suggests that NSAIDs are preferable in musculoskeletal pain where paracetamol/acetaminophen and local preparations have insufficient effect (http://www.nice.org.uk/guidance/cg177). Although NSAIDS are effective analgesics they have a high risk on adverse events (up to a quarter of

hospitalizations due to adverse drug events are the result of NSAIDs). In particular, the increased risk of GI bleeding, the cardiovascular side effects (increased risk of arterial hypertension, heart failure) and worsening of chronic kidney disease highlight that caution is required. If a NSAID is necessary, the lowest dose and the shortest time period should be considered with regular monitoring of side effects. To prevent GI bleeding, a PPI or misoprostol should be prescribed.

Opioids: There is limited evidence in older people for the short term efficacy of opioids in cancer and non-cancer pain such as musculoskeletal pain, including osteoarthritis, low back pain, and various neuropathic pains, such as post-herpetic neuralgia and diabetic peripheral neuropathy. Opioids can be relatively safe used if the prescriber carefully considers their pharmacological properties, if opioids are carefully titrated based on the individual response and if caregivers and patients are counselled regarding potential side effects that could be expected.

Weak opioids: Weak opioids, such as codeine and tramadol, are recommended for use in moderate pain in the WHO pain relief ladder. Literature searches have shown little evidence on the use of these weak opioids in older people. Moreover, these opioids can have side effects which limit their use. Codeine in particularly, can cause constipation, a side effect seen less frequently with tramadol. However, tramadol can cause confusion, reduce the seizure threshold and should be used with caution in patients with other serotonergic drugs (Barber and Gibson 2009). Prospective data suggest that older people require 20% less tramadol than younger adults (Mercadante and Arcuri 2007).

Strong opioids: Studies have demonstrated the efficacy of strong opioids in cancer and non-cancer patients, again there are no studies specifically in older populations. A recent Cochrane review shows that the small mean benefit of non-tramadol opioids for osteoarthritis of knee and hip are contrasted by significant increases in the risk of adverse events (da Costa *et al*. 2014).

Recent reviews of the literature describes the pharmacokinetics of frequently used strong opioids and adverse events (Atkins *et al*. 2013, Tracy and Morrison 2013, Van Ojik *et al*. 2012, Pergolizzi *et al*. 2008).

Morphine: Morphine undergoes substantial hepatic metabolism and renal excretion. Enterohepatic circulation results in Morphine-6-glucuronide (M6G) and morphine-3-glucuronide (M3G) being excreted through bile, faeces and urine several days after the last dose has been taken. M6G contributes to the overall analgesic effect but M3G passes the blood brain barrier and may cause neurotoxic effects. Decreased glomerular filtration rate causes accumulation of those metabolites causing even more severe side effects.

Oxycodone: There is limited evidence that oxycodone has the same efficacy as morphine and is well tolerated in cancer and short term treatment of non-cancer pain.

Fentanyl: Several open label studies and one RCT showed that fentanyl is effective and well tolerated with lower incidence of constipation and nausea than morphine and oxycodone. It is convenient because patches may be changed up to 72 hours which may enhance compliance and make care easier. However because of its high opioid potency, fentanyl should not be started in opioid naïve patients.

Buprenorphine: Buprenorphine is another high potent opioid, available in different formulations (sublingual, parenteral and transdermal). It has similar efficacy and safety in older and younger people. Moreover, the pharmacokinetics are not altered in patients with renal failure.

Hydromorphone: is a high potency opioid, not specifically studied in older people.

Methadone: should, due to its unusual pharmacokinetics, only be prescribed by physicians who are well experienced in pain management.

Tapentadol: could have a therapeutic advantage in the older population due to its unique mechanism of action, low potential for drug interactions, and significantly reduced AE profile. However, because of a lack of evidence, the use is not recommended in frail older people.

Managing the side effects of opioids:

It is important that patients and caregivers are counselled regarding potential side effects. As opioids have similar mechanisms of action, side effects of different opioids may be very similar. Sedation and sleepiness is common, mainly occurs during the first three days of treatment and normally disappears spontaneously. If sedation persists, review of concomitant medication is useful as anxiolytics often have a synergetic effect on the sedative effect of opioids. Where hallucinations and delirium occur, often on the first day of treatment or on dose escalation, combination therapy with opioids and coanalgesics such as gabapentin or amitriptyline should reviewed and stopped where possible. Gastro-intestinal side effects particularly nausea and vomiting, often disappear after a few days but constipation which is a more persistent side effect that should be anticipated and managed by starting laxatives. Another observed side effect in older people is urinary retention and they are also at higher risk of falls and fractures (up to 4 times the incidence compared to people taken NSAIDs) (Solomon *et al*. 2010).

Adjuvant drugs and treatment of neuropathic pain

Co-analgesics such as antidepressants and anticonvulsants are often recommended and especially beneficial for neuropathic pain in older people (http://www.nice.org.uk/guidance/cg173). Tricyclic antidepressants strengthen the inhibitory modulating pathway by increasing the levels of serotonin and noradrenaline. Amitriptyline was the first drug to be used, however its side effects such as postural hypotension, cardiac arrhythmias, urinary retention, glaucoma and worsening cognitive functioning in people with dementia, decrease its usefulness in older people. Special attention should be paid to the co-administration of opioid analgesics with TCAs. This can induce severe side-effects as sedation,

delirium and hallucinations. Nortryptiline, which has fewer anticholinergic side effects may be an alternative. More recently the SNRIs (serotonin and noradrenaline reuptake inhibitors) have been studied as alternatives for TCA. However, SNRIs are safer but have also some burdensome side effects as nausea, hyponatremia, dizziness and sedation; higher doses, sometimes necessary for the analgesic effect, increase the risk of adverse events in older people. The anticonvulsant carbamazepine should be avoided because of the complex pharmacokinetics and the high number of drug interactions. Oxcarbazepine is a 10-keto-analogue and better tolerated. It is well absorbed, metabolised by the liver and the metabolites are excreted by the kidneys. Pregabalin and gabapentin also have an anxiolytic and sedative effect. Adverse events such as dizziness, sedation, difficulties in concentrating and visual disturbances are more frequent in older people. The important difference between pregabalin and gabapentin among both is the bioavailability (90% for pregabalin and 60% for gabapentin). They are both renally excreted and so a reduced dosage is necessary in patients with renal impairment (Schmader *et al*. 2010).

The basic principles of pain treatment in older people are also applicable for the older person with advanced dementia (American Geriatrics Society 2009). However pharmacological treatment is often complicated by swallowing disorders, so alternative methods of administration of drugs should be considered. Patches may be helpful for patients with an expected survival of longer than a few weeks and relatively constant level of pain. However as fentanyl or buprenorphine take a week to obtain a stable plasma level with, treatment with morphine (via syringe driver) is often first choice during the last days of life or during a period of unstable pain experience. Pain treatment should be evaluated and adapted at least every 24 hours until pain relief is obtained.

Ch 159-05 Conclusion

Pain is common in older people also in an older population with dementia. Chronic pain has a significant impact on the quality of life of older people. Epidemiological studies show that musculoskeletal pain due to osteoarthritis is most common. Since pain is often under recognised in the older population, systematic screening and assessment with appropriate tools for the target population, is recommended in the older population. A holistic, multidisciplinary approach may offer meaningful support. It is possible to safely use non-pharmacological treatments and available analgesics, provided the clinician has a good knowledge of the pharmacokinetics and pharmacodynamics of the drugs. In patients with advanced dementia and patients at the end of life, alternative routes of administration of analgesics should be considered. Recognising and managing pain in an older population is challenging but can make a great difference for the older person.